UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/518,988	11/07/2006	Joseph Alexander Lasky	ON/4-32548A	1365

1095 7590 07/18/2008

NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 104/3
EAST HANOVER, NJ 07936-1080

EXAMINER	
RICCI, CRAIG D	

ART UNIT	PAPER NUMBER
4161	

MAIL DATE	DELIVERY MODE
07/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,988	LASKY, JOSEPH ALEXANDER	
	Examiner	Art Unit	
	CRAIG RICCI	4161	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *5-13* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5-13* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/23/2007*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 5-13 are currently pending and the subject of this Office Action. Claims 1-4 are cancelled. This is the first Office Action on the merits of the claims.

Information Disclosure Statement

2. All references have been considered.

Priority

4. The earliest effective filing date afforded the instantly claimed invention has been determined to be 11/07/2006 as to claims 5-13.

Claim Rejections - 35 USC § 112

12. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

13. **Claim 12 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.**

14. Claim 12, which depends from claim 5, recites a method of treating a human subject suffering from pulmonary fibrosis disease wherein the pulmonary fibrosis disease is an interstitial lung disease. The phrase "pulmonary fibrosis disease wherein the pulmonary fibrosis disease is an interstitial lung disease" is not clearly defined by the claim and the specification does not provide a standard for ascertaining the meaning of the phrase. For example, as evidenced by *Reynolds* (Interstitial Lung Diseases; Harrison's Principles of Internal Medicine – McGraw-Hill ed; 14th edition, vol 2, Chapter

259), provided in Applicant's IDS filed 1/23/2007, interstitial lung diseases comprise more than 200 different disorders which include pulmonary fibrosis and more specifically pulmonary fibrosis caused by asbestos and idiopathic pulmonary fibrosis. Thus, one possible interpretation of claim 12 is that the pulmonary fibrosis disease claimed is one that is a species of the genus interstitial lung disease. However, such a reading of claim 12 would not import any additional limitations into claim 5 since it is understood by Examiner, in view of *Reynolds*, that "pulmonary fibrosis disease" as recited by claim 5 is by definition a species of the genus interstitial lung diseases. Alternatively, claim 12 could be interpreted to mean "pulmonary fibrosis disease" wherein the disease is any interstitial lung disease including, but not limited to, the species pulmonary fibrosis.

15. Absent any guidance as to the definition of the phrase ""pulmonary fibrosis disease wherein the pulmonary fibrosis disease is an interstitial lung disease" as recited by claim 12, one of ordinary skill in the art would not be reasonably apprised of the scope of the invention recited by claim 12. Accordingly, the phrase renders the claim indefinite.

16. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

17. **Claims 5-6 and 12-13 are rejected under 35 U.S.C. 112, first paragraph**, because the specification, while being enabling for treating pulmonary fibrosis disease as meaning reducing pulmonary fibrosis in patients with pulmonary fibrosis, does not

reasonably provide enablement for treating individuals in the sense of curative or prophylactic treatment.

18. Additionally, the specification does not reasonably provide enablement for treating all interstitial lung diseases in the sense of reducing any and every interstitial lung disease, including but not limited to pulmonary fibrosis, in any and every patient suffering from an interstitial lung disease as recited by claim 12 as interpreted by Examiner based on the discussion above. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

19. Applicant has given special meaning to the term "treating" that includes "curative treatment and prophylactic treatment" (Page 5). While Applicant has enabled a method of treating pulmonary fibrosis, in the sense that Applicant enables a method for reducing pulmonary fibrosis in humans and the size of the lesion caused by asbestos exposure in mice, curing and preventing the disease are not considered enabled. Additionally, Applicant claims treatment of pulmonary fibrosis disease wherein the pulmonary fibrosis disease is an interstitial lung disease (claim 12). As discussed above, claim 12 is indefinite. However, one reasonable interpretation is that "pulmonary fibrosis disease" comprises any interstitial lung disease including, but not limited to, the species pulmonary fibrosis.

20. Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art

and the amount of experimentation necessary. All of the Wands factors have been considered, with the most relevant factors discussed below.

21. Nature of the invention: The rejected claims are drawn to methods for treating pulmonary fibrosis disease (claim 5), pulmonary fibrosis disease caused by asbestos (claim 6), pulmonary fibrosis disease wherein the disease is an interstitial lung disease (claim 12), and wherein the disease is an idiopathic pulmonary fibrosis (claim 13). More specifically, the claims are drawn to methods of treatment comprising administering a dose, effective against pulmonary fibrosis, of the compound of formula I (hereinafter COMPOUND I, also known as imatinib or Gleevec or STI571) or a pharmaceutically salt thereof.

22. Breadth of the claims: Taken together with the specification, the claims imply that administering COMPOUND I will 1) prevent pulmonary fibrosis disease and 2) will cure pulmonary fibrosis disease in an individual that has pulmonary fibrosis disease. Moreover, the claims imply that administering COMPOUND I will also prevent and cure any interstitial lung disease. As evidenced by *Reynolds* (Interstitial Lung Diseases; Harrison's Principles of Internal Medicine – McGraw-Hill ed; 14th edition, vol 2, Chapter 259), provided in Applicant's IDS filed 1/23/2007, interstitial lung diseases comprise more than 200 different disorders including pulmonary fibrosis caused by asbestos and idiopathic pulmonary fibrosis. Thus, the claims imply that administering COMPOUND I will additionally prevent and cure over 200 different disorders broadly categorized as interstitial lung diseases. However, there is no evidence that the 200 or more interstitial lung diseases share similar etiologies or pathologies that can be treated using a single

process. While it is clear that at least 3 of the interstitial lung diseases involve PDGF, there is nothing to suggest that PDGF is involved in the other 197 plus interstitial lung diseases.

23. Guidance of the specification/The existence of working examples: Applicant provides as evidence that administration of COMPOUND I will prevent and cure over 200 interstitial lung diseases and specifically pulmonary fibrosis disease caused by asbestos and idiopathic pulmonary fibrosis, two examples. The first example "suggest that COMPOUND I has an unexpected potential for the treatment of pulmonary fibrosis" and the second shows that "COMPOUND I administration reduces the size of the lesion" caused by asbestos exposure in mice.

24. The state of the art and the Predictability of the art: As evidenced *by Lasky and Brody* (Environ Health Perspect. 106(S4):751-62, 2000), provided in Applicant's IDS filed 1/23/2007, "the clinical outcome for the vast majority of patients with IPF [interstitial pulmonary fibrosis] remains poor. Published statistics indicate that our lack of ability to intervene in the fibrotic process leads to premature death. In a retrospective study published 20 years ago, *Carrington et al* reported on the natural history and treated course of 53 patients with usual interstitial pneumonitis (UIP), and found that only 50% remained alive after 5 years and 18% after 10 years following their diagnosis. More recent 5- and 10-year Kaplan Meier survival analyses figures were 53 and 20%, respectively, in 85 subjects with UIP followed by the United States Armed Forces Institute between 1974 and 1993 according to Travis et al. The lack of improvement in IPF mortality over the 20-year interval between the Carrington and Travis reports clearly

indicates that currently employed medical regimens are of marginal use." Thus, a treatment to cure and prevent the 200 plus diseases that qualify as interstitial lung diseases, and more specifically to cure and prevent pulmonary fibrosis caused by asbestos and idiopathic pulmonary fibrosis, would be unpredictable.

25. The amount of experimentation necessary: Considering the breath of the claims, the state of the art as discussed above, the current poor prognosis in patients and lack of effective medical regimens, and the high unpredictability in the art as evidenced therein, combined with the lack of guidance provided in the specification, one of ordinary skill in the art would be burdened with undue experimentation to practice to the invention commensurate in the scope of the claims.

Claim Rejections - 35 USC § 103

26. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

27. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

28. **Claims 5-6 and 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over *Hasselbalch* (Am J Hematol 68(1):63-64), *Lasky et al* (Am J Respir Crit Care Med 157:1652-1657, 1998) and *Bonner et al* (Am J Physiol Lung Cell Mol Physiol 274:L72-L80, 1998).**

29. Claim 5 is drawn to methods for treating pulmonary fibrosis in human subjects using 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide (also known as imatinib, Gleevec, STI571, and hereinafter "COMPOUND I") or a pharmaceutically salt thereof. Claims 6 and 12-13 are drawn to the method of claim 5 wherein the pulmonary fibrosis disease is induced by asbestos (claim 6), is an interstitial lung disease (claim 12), or is an idiopathic pulmonary fibrosis (claim 13).

30. *Hasselbach* teaches that COMPOUND I is an inhibitor of the platelet derived growth factor receptor (PDGF-R). Additionally, *Hasselbach* teaches the use of COMPOUND I in the treatment of diseases associated with overexpression of the PDGF-R. Specifically, *Hasselbach* teaches that "preliminary data indicate that STI571 [i.e., COMPOUND I] has significant activity in conditions with overexpression of the PDGF-receptor" and proposes that "by targeting the PDGF-receptor... STI571 might have a clinically relevant activity" (Page 63, Column 2, Paragraph 3). However, *Hasselbach* does not teach the use of COMPOUND I in the treatment of the various pulmonary fibrosis diseases encompassed by claims 5-6 and 12-13.

31. As taught by *Lasky et al*, PDGF-receptor expression is increased following exposure to asbestos in a well characterized rat model of asbestos-induced lung fibrosis

(Page 1653, Column 1, Paragraph 2). Furthermore, *Lasky et al* suggest that the increase in PDGF receptor expression "are relevant to lung injury in humans" (Page 1656, Column 1, Paragraph 3).

32. Furthermore, as taught by *Bonner et al*, PDGF-receptor expression is induced by interleukin-1β (IL-1β) in a rat model of pulmonary fibrosis (abstract). Moreover, *Bonner et al* teach that "in humans, alveolar macrophages from patients with **idiopathic pulmonary fibrosis** or individuals exposed to asbestos release enhanced levels of IL-1β. PDGF-Rα gene expression by IL-1β occurs 4 h after treatment of lung myofibroblasts in vitro, and cell-surface PDGF-Rα appears within 12 h" (Pages L77-L78, emphasis added).

33. Thus, the prior art teach that COMPOUND I is useful in the treatment of conditions wherein the PDGF-R is overexpressed, and furthermore that the PDGF-R is overexpressed in pulmonary fibrosis, pulmonary fibrosis induced by asbestos, and idiopathic pulmonary fibrosis, all of which are examples of interstitial lung diseases in view of *Reynolds* as discussed above. Accordingly, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made to use COMPOUND I to treat an interstitial lung disease such as pulmonary fibrosis, idiopathic pulmonary fibrosis, and pulmonary fibrosis induced by asbestos.

34. **Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over *Hasselbalch* (Am J Hematol 68(1):63-64), *Lasky et al* (Am J Respir Crit Care Med 157:1652-1657, 1998) and *Bonner et al* (Am J Physiol Lung Cell Mol Physiol**

274:L72-L80, 1998) as applied to claims 5-6 and 12-13 above, in further view of *Raghu et al* (Am Rev Respir Dis 144(2): 291-296, 1991).

35. Claim 7 is drawn the method of instant claim 5 wherein COMPOUND I is administered once daily for a period exceeding 3 months.

36. However, the prior art discussed above do not teach the daily administration of COMPOUND I for a period exceeding 3 months in the treatment of pulmonary fibrosis.

37. It is well known in the art that fibrosis is a chronic condition that requires ongoing treatment. More specifically, it is well known in the art that regimens for the treatment of conditions such as pulmonary fibrosis are routinely continued for time periods in excess of 3 months. As taught by *Raghu et al*, treatment of pulmonary fibrosis using corticosteroids (the mainstay in the treatment of pulmonary fibrosis) requires daily administration for more than 3 months. Accordingly, a person of ordinary skill in the art – recognizing that fibrosis is not an acute syndrome and in view of *Raghu et al* – would have known to administer COMPOUND I and its pharmaceutically acceptable salts in the treatment of fibrosis daily for a period exceeding 3 months.

38. **Claims 5 and 8-11 rejected under 35 U.S.C. 103(a) as being as being unpatentable over *Zimmermann et al* (WO 99/03854) in view of *Rice et al* (Am J Pathology 155(1):213-221, 1999).**

39. Claim 5 is drawn to methods for treating pulmonary fibrosis in human subjects using 4-(4-methylpiperazin-1-ylmethyl)-N-[4-methyl-3-(4-pyridin-3-yl)pyrimidin-2-ylamino)phenyl]benzamide (also known as imatinib, Gleevec, STI571, and hereinafter "COMPOUND I") or a pharmaceutically salt thereof. Claims 8-10 are drawn to the

method of claim 5 wherein COMPOUND I is in the form a pharmaceutically acceptable acid addition salt (claim 8), more specifically the monomethane sulfonate salt (claim 9), and even more specifically the beta crystal form of the mesylate salt (claim 10).

40. *Zimmermann et al* teach COMPOUND I, more specifically the beta crystal form of the mesylate salt of COMPOUND I, in the treatment of disease including fibrosis (Page 11, Paragraph 1). More specifically, *Zimmermann et al* teach that COMPOUND I and the beta crystal form of the mesylate salt of COMPOUND I "may especially be used for the treatment of diseases which respond to an inhibition of the PDGF receptor kinase" (Page 11, Paragraph 1). However, *Zimmermann et al* do not teach the use of COMPOUND I or its salts in the treatment of pulmonary fibrosis.

41. *Rice et al* teach that specific inhibitors of PDGF receptor tyrosine kinase reduce pulmonary fibrosis in rats (Title). More specifically, *Rice et al* teach that "PDGF-R-specific... tyrosine kinase inhibitors... block rat lung myofibrobast mitogenesis *in vitro* and inhibit the progression of pulmonary fibrosis *in vivo*" (Page 218, Column 1, Paragraph 1). Accordingly, it would have been obvious to a person of ordinary skill in the art to use COMPOUND I, more specifically the beta crystal form of the mesylate salt of COMPOUND I as taught by *Zimmermann et al*, in the treatment of pulmonary fibrosis, since *Zimmermann et al* teach that COMPOUND I is useful in the treatment of fibrosis and diseases which respond to inhibition of the PDGF receptor kinase and since *Rice et al* teach that pulmonary fibrosis is a disease which responds to an inhibition of the PDGF receptor kinase.

42. Claim 11 is drawn to a method of administering to a person suffering from pulmonary fibrosis a daily dose of 200 mg to 800 mg of the beta crystal form of the mesylate salt of COMPOUND I free base. *Zimmermann et al* teach "that all indicated inhibitory and pharmacologicial effects are also found with the free base" (Page 16) and that "daily doses of about 1-2500 mg, preferably 1-1000 mg, especially 5-500 mg, are administered to warm-blooded animals of about 70 kg bodyweight" (Page 17). Where the claimed ranges "overlap of lie inside ranges disclosed by the prior art" a *prima facie* case of obviousness exists. *In re Wertheim*, 541 F.2d 257, 191 USPQ 90 (CCPA 1976). See also MPEP 2144.05. The instant range of 200-800 mg clearly overlaps the especially preferred range of 5-500 mg taught by *Zimmermann et al*. Accordingly, it would have been prima facie obvious to one of ordinary skill in the art to administer a daily dose of 200-800 mg of COMPOUND I in the beta crystal free base form to an adult human in the treatment of pulmonary fibrosis.

Double Patenting

43. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140

F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

44. Claims 5-9 and 12-13 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-4, 6-7 and 10 of copending Application No. US 2006/0154936 A1 in view of *Enson et al* (Trans Assoc Am Physicians 88:248-255, 1975), *Espinosa et al* (Mayo Clin Proc 68(8):778-782, 1993) and *Voelkel and Tudor* (Eur Respir J 8:2129-2138, 1995).

This is a provisional obviousness-type double patenting rejection.

45. Claims 10, 4 and 7 of the '936 Application recite the method described by instant claims 5-9 and 12-13. Specifically, claim 10 recites the use of COMPOUND I; claims 3-

4 recite daily administration of 100 to 1000 mg of COMPOUND I for a period exceeding 3 months; and claims 6 and 7 recite the monomethanesulfonate salt of COMPOUND I. However, the '936 Application recites the method in the treatment pulmonary hypertension rather than in the treatment of pulmonary fibrosis diseases as recited by instant claims 5-9 and 12-13.

46. It would have been obvious to a person of ordinary skill in the art to use the method taught by the '936 application in the treatment of pulmonary fibrosis diseases as recited by the instant application for the following reasons:

47. First, as taught by *Enson et al*, pulmonary hypertension is a complication of interstitial lung diseases generally and, as taught by *Espinosa et al*, may also be caused by idiopathic pulmonary hilar fibrosis specifically. More specifically, *Espinosa et al* teach that "pulmonary vascular causes of chronic pulmonary hypertension include... pulmonary hilar fibrosis" (Page 781, Column 1, Paragraph 1). Given this association, one of ordinary skill in the art would have been motivated to treat an underlying cause of pulmonary hypertension - namely, pulmonary fibrosis diseases - in the treatment of pulmonary hypertension. Accordingly, it would have been obvious to a person of ordinary skill in the art to use COMPOUND I in the treatment of pulmonary fibrosis diseases.

48. And second, *Voelkel and Tudor* teach that, similar to the pulmonary fibrosis diseases recited by instant claims 5-7 and 12-13, PDGF is implicated in the pathology of pulmonary hypertension (entire document). Since PDGF is involved in both pulmonary hypertension and pulmonary fibrosis diseases, it would have been obvious to one of

ordinary skill in the art at the time the invention was made to use the method for treating pulmonary hypertension comprising administering a compound recognized as a PDGF inhibitor, as recited by the '936 Application, to treat related pulmonary disorders that also involve elevations in PDGF and respond to its inhibition.

49. And third, in view of *Enson et al* and *Espinosa et al* which teach that pulmonary hypertension and pulmonary fibrosis disease are associated, it is evident that the treatment group of the '936 Applicant and the instant application are identical. Furthermore, since PDGF is involved in the progression of both pulmonary hypertension and pulmonary fibrosis diseases, the method recited by the '936 application which utilizes a recognized PDGF inhibitor in the treatment of pulmonary hypertension would inherently treat pulmonary fibrosis diseases as well.

50. Claims 10 and 11 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 3-4, 6-7 and 10 of copending Application No. US 2006/0154936 A1 in view of *Enson et al* (Trans Assoc Am Physicians 88:248-255, 1975), *Espinosa et al* (Mayo Clin Proc 68(8):778-782, 1993) and *Voelkel and Tudor* (Eur Respir J 8:2129-2138, 1995) as applied to claims 5-9 and 12-13 above, in further view of *Zimmermann et al* (WO 99/03854).

51. As discussed above, claims 5-9 and 12-13 of the instant application are rejected on the ground of nonstatutory obvious type double patenting as being unpatentable over the '936 application. However, the prior art does not teach the beta crystal form of the

mesylate salt as recited by instant claim 10, nor does it teach the free base as recited by instant claim 11.

52. As discussed above, *Zimmerman et al* specifically teach COMPOUND I as well as COMPOUND I in the form of a pharmaceutically acceptable acid addition salt, more specifically the monomethane sulfonate salt, and even more specificially in the beta crystal form of the mesylate salt, in the treatment of various diseases including fibrosis and diseases which respond to inhibition of the PDGF receptor. Accordingly, one of ordinary skill in the art would have recognized that COMPOUND I and the beta crystal form of its mesylate salt were equivalents. Thus, it would have been obvious to a person of ordinary skill in the art to use the beta crystal form of the mesylate salt of COMPOUND I in the '936 application.

53. Additionally, as discussed above, *Zimmermann et al* teach "that all indicated inhibitory and pharmacologicial effects are also found with the free base" (Page 16). Accordingly, it would have been obvious to a person of ordinary skill in the art to the use the free base of the COMPOUND in the '936 application.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to CRAIG RICCI whose telephone number is (571)270-5864. The examiner can normally be reached on Monday through Thursday, and every other Friday, 7:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Patrick Nolan can be reached on (571) 272-0847. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/CRAIG RICCI/
Examiner, Art Unit 4161

/Patrick J. Nolan/
Supervisory Patent Examiner, Art Unit 4161